UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/936,857	09/24/97	ECKSTEIN	F 228213

HM11/1127

LYON & LYON
FIRST INTERSTATE WORLD CENTER
633 WEST FIFTH STREET
SUITE 4700
LOS ANGELES CA 90071

EXAMINER	
LEGUYADER, J	
ART UNIT	**PAPER NUMBER**
1635	9

DATE MAILED: 11/27/98

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☐ This application has been examined ☒ Responsive to communication filed on 9/28/98 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), ___ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☒ Claims 44-57 are pending in the application.
   Of the above, claims _____ are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 44-57 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____ ; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 44-46, 48, 50-57 are rejected under the judicially created doctrine of double patenting over claims 1-26 of U. S. Patent No. 5,672,695 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: The claimed invention is drawn broadly to a method of cleaving an RNA target via a ribozyme having modified nucleotides, the modification comprising any modifier group at the 2' position of the ribose, where the modifier can be any halo or any amino. Patent '695 is drawn to ribozymes with modified nucleotides, the modification being halo or disubstituted amino at the 2' position of the ribose. The ribozyme of the method claims herein overlap in scope with those claimed in patent '695. The only difference between the claims of the instant application and the patent cited is that the instant application claims a method of ribozyme cleavage, whereas the patent is drawn solely to the ribozyme. However, the method of cleaving target is an obvious use for a ribozyme since this the intent when making the compound.

Furthermore, there is no apparent reason why applicant was prevented from presenting claims corresponding to those of the instant application during prosecution of the application which matured into a patent. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

Claims 44-57 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claimed invention as now claimed in applicants 9/28/98 amendment is drawn to a method of cleaving any RNA via any ribozyme motif wherein the ribozyme is composed of at least one modified nucleotide, the modification comprising any modifier group replacing the 2' hydroxy of the ribose sugar. Further dependent claims limit the claimed invention to where the modifier group is any halo or any amino, and where the target RNA is viral. The context of the cleavage is not specified by the claim and thus reads broadly on ribozyme cleavage in any in vitro and in vivo context.

The specification as filed teaches only ribozymes with modified nucleotides having 2'-halo and 2'-amino cleaving RNA, and with cleavage of HIV LTR RNA in a cell free system. No ribozyme cleavage in cells is taught, although a stability against nuclease degradation for the ribozymes in cells in culture was conducted. No accompanying data on target cleavage was mentioned or provided. No other guidance is provided for delivery of ribozymes to cells to cleave

target in any context is provided. No Guidance is provided as to what other modifier groups and at what positions in ribozyme motifs such modifiers can be tolerated and provided for a functional ribozyme, and further one that could be delivered to cells in culture or in vivo (whole organism) and still further cleave target.

Note the state of the art for the construction of ribozyme which may be delivered and cleave target in cells in culture and in a whole organism remain highly unpredictable due to RNA secondary and tertiary structure and the corresponding ability of the target to be accessible in cells, and the issues concerning delivery to cells (see Branch). The specification as filed fails to provide any general or particular guidance to resolve the unpredictable factors concerning the engineering and delivery of ribozymes to cleave target in cells.

Several areas of de novo experimentation would have to be engaged to practice the invention as broadly claimed. To the extent that the ribozymes of the claims are drawn to having any modifier, no guidance is provided as to what other modifiers would be applicable and where within any catalytic motif of any ribozyme. Each ribozyme motif have core positions for which substitutions will not be tolerated. Furthermore, the ribozyme must be engineered such that they would cleave any target in any context. No guidance is provided in the specification as filed for the determination of every or any ribozyme cleavage site, even for any viral target RNA. Still further, the method claims call for cleavage to occur in any context in vivo. No general delivery schemes are known for ribozymes, and further for those with modifier groups, such that hey may find and cleave target. All applicants have done is shown nuclease resistance in cells, but do not show that the ribozymes claimed, even for those shown in vitro, can cleave target in cells, or

further be delivered and cleave target in a whole organism. To do so as claimed and recited in this paragraph would require trial and error experimentation since the specifcation as filed fails to provide any guidance in the known unpredictable factors concerning the engineering and delivery of ribzoymes for cleavage of a desired target in cells.

Any inquiry concerning this communication should be directed to John L. LeGuyader at telephone number (703) 308-0447. Please note that the examiner's compressed workweek day off is every Friday.

John L. LeGUYADER
November 24, 1998

JOHN L. LeGUYADER
PRIMARY EXAMINER
GROUP 1800
1600